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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/030,985	02/26/98	FALO JR L	214001-00648

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EXAMINER	
PELLEY,R	
ART UNIT	**PAPER NUMBER**
1644	9

DATE MAILED: 02/02/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/030,985	Falo And Celluzzi
Examiner	**Group Art Unit**
Ronald Pelley	1644

☒ Responsive to communication(s) filed on *Nov 25, 1998*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-36* is/are pending in the application.

Of the above, claim(s) *1-12, 16, and 25-36* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *13-15 and 17-24* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 7

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. To aid in correlating any papers for this application, all correspondence regarding this application should be directed to Group Art Unit 1644, Group 1640, Technology Center 1600/2900.

2. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

3. Applicant's election with traverse of Group I, claims 1-7 in Paper No. 8 of 27 November, 1998 is acknowledged. The traversal is on the grounds that a proper search of the Group II claims would necessarily reveal references relating to Group IV method of treating a patient to stimulate a CTL response. This is not found persuasive because of the same reasons set forth in paper No. 6. Further, a prior art search also requires literature searches. It would be unduly burdensome to search more than one invention in one application.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 13-24 are being examined in this application. Claims 1-12 and 25-36 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a nonelected invention.

4. Applicants election without traverse to prosecute the formulations and compositions recited in claims 13 and 20 as "dendritic cells", in claims 13 and 20 as tumor cells and in claim 15 as "lung carcinoma cells" is acknowledged. Claims 14-15, 17-19 and 21-24 are readable on the elected embodiment. Claim 16 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a nonelected species. Claims 13-15 and 17-24 are being examined in the application.

5. The specification on page 1, line 2 should be amended to reflect the priority claimed under 35 USC 119(e) to U.S. Provisional Application No. 60/039,472.

6. The following are quotations of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 13 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13 and 20 as recited are vague and indefinite in the use of "products of co-culture" particularly given the open nature of the transitional phrase "comprising". The metes and bounds of these "products" is so defined in specification (page 8, lines 19-22, "cells that have become fused together, cells that are not fused, and cellular components") so as to encompass any virtually any matter including any product of the cellular metabolism of tumor and dendritic cells. This in unacceptably indefinite. For the purposes of examination these claims are given their broadest possible interpretation.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 13-14 and 17-24 are rejected under 35 U.S.C. 103 as being unpatentable over Guo et al. (Ref. C in IDS) in view of either Murphy et al. (U.S. Patent No. 5,788,963) or Steinman et al. (U.S. Patent No. 5,851,756).

Guo et al. teach that tumor cells escape the immune response because of alteration of antigen processing results in an inability to present tumor antigen properly (in particular, p 518, 1st col. 1st para.). They also teach co-culture of APC with tumor cells with fusion of APC with tumor as a way of surmounting antigen processing problems (in particular, page 518, 1st col., 2nd para.). They teach a ratio of 10 first cells (antigen presenting B cells) to each second cell (tumor cell) in fusion culture (in particular, page 520, footnote 11). Injection of this product of co-culture resulted in effective induction of tumor immunity (Figure 2) which required $CD8^+$ lymphocytes. The claimed invention differs from the reference teaching only by the recitation of dendritic cells as the APC fusion partner.

Steinman et al. teach a method for in vitro proliferation of dendritic cell precursors and their use to process antigens for induction of immune responses (entire document). In particular they teach that the product of their method is dendritic cells bearing processed antigen or processed

antigen from dendritic cells (col. 3, line 62 to col. 4 line 60; col. 5, lines 52 to 56; col. 5, line 66 to col. 6 line 8; col. 6 lines 49-54 and 60-62; col. 7, lines 18-21; col. 17, lines 65-67; col. 18, line 61 to col. 9, line 2; col 19 and line 45 to col. 20, line 3). They teach that the dendritic cell processed antigen product can be the result of cell to cell contacting or co-culture including phagocytosis (in particular col. 18, lines 37-40; col. 19, line 45 to col. 20, line 19; and exemplified in Figure 12) and the mixed lymphocyte reaction (in particular, col. 17, lines 40-42, Figures 4-6 & 18). This process cumulates in complexing processed antigen with MHC (in particular, col. 18, lines 37-40 and col. 20 lines 11-19) to result in a product capable of stimulating T cells including $CD8^+$ CTL's (in particular, col. 21, lines 22-37 and 58-67). They teach that this has implications for viral and tumor antigens (in particular, col. 18, lines 5-9). They teach that in certain cases, this dendritic cell processed antigen may be soluble (col. 22, lines 42-54). They teach the distribution of dendritic cells in organs such as skin, lymph nodes and spleen and teach their production from precursors (in particular col. 1, lines 32-52 and col. 2, lines 6-41). They teach the utility of culture of dendritic cells to in making a processed antigen product for the purpose of inducing a therapeutic immune response (in particular, col. 5, lines 46-51 and 64-65, col. 6, lines 9-13, col. 7, lines 5-12 and 34-36; and col. 22, line 55 to col. 23, line 3) including formulation in carriers such as physiological saline or other injectable liquids (col. 22, lines 61-63).

Murphy et al. teach the utility of immunotherapy of cancer (Section 2.2, col. 1-2) and the importance of dendritic cells as APC (in particular, col. 2, lines 48-64) and their superiority to monocytes and B cells as APC (in particular, col 2, lines 42-47). In particular (col. 3, lines 12-18, col. 5, lines 33-36 and col. 10, lines 38-67) they teach a preparation of dendritic cell APC with cancer antigen suitable for administration to a human for the purpose of treating cancer. They teach the isolation and expansion of dendritic cells (Section 5.1, col. 5-8), that crude cell lysates work as well as purified antigen (in particular, col. 8, lines 42-54) and that cultivation of such particulate antigen with dendritic cell APC induces CTL (in particular Figures 3 & 5 and Section 6.6, cols. 15 & 16).

One of ordinary skill in the art at the time the invention was made would have been motivated by the teachings of Steinman and Murphy that cultured dendritic cell were the best way to process antigen and induce an immune response and the teaching of Guo that co-culture of antigen presenting cells with tumor cells followed by injection generated strong tumor immunity to employ the dendritic cells of Steinman or Murphy as a source of antigen processing cells in the method of Guo at a ratio of about 6:1 APC's to tumor cells in the expectation of making a better vaccine for cancer. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. Claims 13 and 15 are rejected under 35 U.S.C. 103 as being unpatentable over Guo et al. (Ref. C in IDS) in view of either Murphy et al. (U.S. Patent No. 5,788,963) or Steinman et al. (U.S. Patent No. 5,851,756) as applied to claim 13 above and further in view of Zeid et al. (1993, U).

Gao et al., Steinman et al. and Murphy et al. have been discussed supra. The claimed invention differs from the reference teaching only by the recitation of co-culture of lung carcinoma cells with dendritic cells.

Zeid et al. teach that the survival of patients whose lung carcinomas contained high densities of dendritic cells was higher than survival of those patients whose tumors had few dendritic cells (in particular, Abstract, last 3 sentences). They concluded that the density of the antigen presenting dendritic cells in lung cancer was related to subtype, tumor differentiation and that a high APC dendritic cell density was associated with survival. In particular they teach (page 342, 1st col., last para.) that death of tumor cells in vivo was associated with a high density of dendritic cells and lymphocytes implying the effect of sensitized T lymphocytes acting specifically against the target tumor cells.

One of ordinary skill in the art at the time the invention was made would have been motivated by the teaching of Zeid equating dendritic cell APC function with survival to employ lung carcinoma cells as a source of antigen for antigen presentation by the dendritic cells of Steinman or Murphy using the method of Guo to produce a cancer vaccine in the expectation of making a better vaccine for lung cancer. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ronald P. Pelley whose telephone number is (703) 308-9343. The examiner can normally be reached Monday through Friday from 8:30 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the Supervisory Patent Examiner is Christina Chan at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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Patent Examiner
Group 1640

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2/1/99